Aus dem Pathologisch-Anatomischen Institut der Universität Basel
(Vorsteher: Prof. Dr. A. Werthemann)
Arbeit unter Leitung von Prof. Dr. S. Scheidegger

CONGENITAL MERISTOMA

Report of a Case with Autopsy

INAUGURAL-DISSERTATION
zur Erlangung der Doktorwürde der Medizinischen Fakultät
der Universität Basel

vorgelegt von
ROBERT S. HERRON
von Long Beach, Kalifornien

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VERLAG P. G. KELLER - WINTERTHUR

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Tag der Promotion: 16. November 1962

There is a twofold basis for presenting this case. As Wells showed in his review, congenital malignant tumors manifest at birth are not common. The second ground is that it should serve as a contribution, albeit small, to the pool of information on childhood tumors. The case for this pool is well stated by Andersen: "Although childhood cancer is increasing in relative importance, the absolute number of cases remains few, and further knowledge of childhood tumors as a whole, and of the group of uncommon tumors in particular, requires pooling of experience."

Pack and Ariel note the good point that the carcinogen producing a manifest resulte in nine months must be "extremely potent". Wells points out the contrast of congenital tumors and Gaisford that of childhood tumors with the ordinary malignant growth of the adult, be it human or animal, which arises only after the organism has lived a large fraction of its life span exposed to the action of exciting agents.

The meristomas are tumors whose lack of (or loss of) differentiation and diffuse structure preclude classification either with epithelial or mesenchymal categories. The description is graphic in describing the histologic similarity of the tissue with that of the embryonic tissue of plants, meristem. Fischer-Wasels makes a convincing case for his choice of the word, citing the confusion wrought by the usage of "sarcoma" as a catch-all for various and sundry tumors of undifferentiated nature. His examples include the numerous false reports of induction of a sarcoma by a carcinoma, and the mistaken classification of adenomas of the pituitary, nephroma embryonale, as well as neuroblastoma of the sympathicus as round-cell sarcomas.

Willis notes the disagreement between various authors over another tumor, often anaplastic, whose diffuse structure and poor differentiation have caused a large amount of strite and confusion. Descriptions range from various carcinomas through sarcomas. Lüdin also cites this same tumor and grounds the use of meristoma for it.

In discussing malignant neoplasms of the soft somatic tissues, Pack and Ariel state, "Such tumors have frequently been described by the nondescript generic heading of sarcoma and have been lumped into this nosologic repository without effort to identify, further subdivide and thereby to learn and conquer the various subdivisions." The arguments of Fischer-Wasels are as valid now as then.

Our tumor lacks differentiation and has diffuse structure. It is not possible to responsibly call it either carcinoma or sarcoma. Since it looks like meristem we have classed it as a meristoma. The term is concise, consequently applied, and graphically descriptive. Unjustified generic typing is avoided.

Anamnesis

The child, second of a German-Swiss couple, was born on 19 February 1959. Familial history and course of the pregnancy are without significance. The tumor was noted at delivery as a tuberous growth on the right side of the neck.

During the first ten days of life, the breast-fed child nursed adequately, though it failed to show a good weight gain. After the tenth day, a progressive effort in nursing was noted. At about two weeks of age a marked decrease in the motility of the upper extremities, in particular that of the right arm, was noted. An increasing paralysis became evident and the child was admitted to the Children's Hospital of the University of Basel on 12 March 1959. Within hours after admission flaccid paralysis of the left arm followed that of the right. On the following day the infant hardly moved both lower extremities. There were no reflexes demonstrable. A röntgenogram of the cervical vertebrae and of the upper extremities was negative. There was a leucocytosis of 20,000. R.B.C.'s were 4.3 million per cubic millimeter and reticulocytes were 22 ‰. Urine was normal. Exitus lethalis at 23.10 on 13 March was attributed to central circulatory collapse.

Post-Mortem

S. N. 412/59

Other than the tumor on the right side of the neck, there were no other discernable external anomalies on the 49 cm long child. The neck tumor consisted of several cauliflower-like, grey-white and dark brown nodules. The consistency was in part soft, in part firm. The nodules could be easily moved in conjunction with the skin. The neck tumor(s) were, macroscopically, restricted to the skin. Tongue, thyroid, thymus, pharynx and trachea were macroscopically free of tumor or anomalies, as were both brachial plexi which were dissected. There were no irregularities of structure in any of the internal organs, other than a number of isolated, unsharply demarcated soft nodules in the intestinal mesentery.

In the area of the cerebellum and medulla oblongata, particularly on the anterior side in the leptomeninx were numerous, seemingly compact, grey-white tumors. Such tumors extended also into the vicinity of the pedunculi cerebri up to the region of the pituitary. There was also a pea-sized, lightly roughened thickening of the dura in the area of the foramen magnum. The tumor filled out the entire space of the dural sack about the spinal cord, compressing and partially infiltrating the cord as well as the spinal meninges.

A general stagnation of blood in the parenchymatous organs, general fluidity of the blood, and a somewhat dilated right ventricle were noted.

Histology

Microscopically, the skin of the neck showed extensive infiltration with tumor. Essentially composed of small cells, the tumor was strongly dissociated, with seemingly spindle-like cells. For the most part the tissue was loose. Only

occasionally were vascularization and fiber formation seen. Some elements suggested, through their spindle-form, a mesenchymal element.

In the brain were multiple foci of tumor similar to that of the tumor in the skin. The cells were relatively small, of spindle-form, rarely round. Nuclei were neither large nor rich in chromatin; however, numerous mitoses were seen. The structure was neither pure mesenchymal nor epithelial in nature. The tissue was foreign to the brain. It infiltrated the leptomeninx and the cortex, following primarily the pial vessels. The tumor cells were small, spindle-shaped and occasionally round. The reticular framework was exceptionally well developed and was so extensive that virtually all of the tumor cells were surrounded by reticular fibers.

Of the various groups of lymph nodes examined, only those in the lumbar region showed tumor cells. These cells were similar to those of the neck and those found in the brain.

Also examined histologically for tumor, but with negative results were: kidneys, heart, liver, thymus, spleen, adrenals, pancreas, thyroid, and the skeletal muscle of the extremities.

The skeletal muscle did, however, show a partial degeneration of the fibers. In numerous places were foci of inflamatory response with fine proliferation of connective tissue.

Resume of Findings

The tumor cells which were found in the central nervous system and in the lumbar lymph nodes showed a uniform histological character, i. e., a high degree of undifferentiation and diffuse structure.

Careful and complete autopsy failed to show other tumor sites. The CNS involvement by tumor explained the clinical course, adequately supported by negative peripheral causes of neurological defects.

Discussion

That the tumor, seen at delivery and lethal through its metastases in 23 days post partum, is a genuine congenital malignant tumor needs, I feel, no particular discussion.

However, the assumption of a branchial origin deserves some consideration. When such authorities as A. P. Stout and R. A. Willis emphasize the rarity of a genuine branchial cancer, one does well to make such a diagnosis with caution. In the report of Crile and Kearns one of the authors should have had the unusual good fortune to have observed twenty-eight malignant growths of branchial origin. This report of so many cases seen by one man contrasts sharply with those of other very experienced authors. Carp and Stout had but four out of a series of 1,538 cancers (of a total of 3,961 tumors seen over

a period of ten years) which they ventured to describe as "were thought to have a branchial origin". Willis had but two for which he wagered even to say "probable" as to branchial origin. The disparity suggests an appreciable difference in criteria used for establishing a malignancy as branchial in origin.

Willis with his two probables cites one other report (Cole and Edgerton) as the sole case he will accept as definately shown. This may well represent an extreme on the conservative side, but he makes a strong case for his conservatism. Broders joins Willis as do Carp and Stout (who cite a number of other like-minded authors) in viewing the greater number of the reported cases of branchial cancer as probable cervical metastases of primary tumors which escaped detection. Neel's examination of 319 branchial cysts and sinuses (pathological specimens) failed to show any evidence of cancer.

Willis goes further and stipulates this condition for assumption of branchial origin of a cervical malignancy: "Only complete and careful necropsy, to exclude primary tumors in all possible sites can identify a cervical growth as of branchial origin." This condition was met in our case, and we deal here with a primitive malignant growth of branchial origin.

The congenital malignant tumors present a small and stimulating group of the tumors of early childhood. The fact that the cancerogen has been capable of working its effect in so short a time gives rise to interesting speculations as to etiology and pathogenesis.

Wells made an important contribution by showing, with his critical review, how few of the previously reported "congenital" malignant growths could be accepted. He unearthed such cases as a repeatedly cited cancer of an infant—the "infant" in this particular case being 17 years of age! From 255 reported cases he gleaned 66 which he felt he could pass on as certain. To these he added his four neuroblastomas. He mentions, too, finding the usage of the description "congenital" for tumors arising in adults (e. g. in moles, birthmarks) as confusing. I have a similar problem when confronted with the statement of Andersen: "The fact that embryonal tumors may not be discovered until later childhood or adult life is no argument against their embryonal origin." At the very least it is an argument, and to be sure, not such a bad one at all in the case of adult cancers. Nicholson's "Birth is a mere incident in the life of the individual; therefore all tissues and tumors are essentially congenital" fails to impress me as reconcilable with the fact that the tumors of the very young show clear differences from the adult tumors. No one seems to find specialization in pediatrics and in geriatrics illogical. The young organism is not the same as the old organism and lumping of the two together would show little promise in helping to get to the roots of the cancer problem.

The increasing interest exhibited in the last two decades in childhood tumors has gained impetus from the relative increase in importance of cancer in child mortality. As Pack and Ariel point out, "Twenty years ago cancer was not even listed in the group of the ten most frequent causes of death in

children." Gaisford mentions an absolute increase in leukemias, but agrees with most other authors that the main reason for the prominence of cancer today are the inroads made on other causes of infant mortality by the development and use of chemotherapeutica. Dargeon cites, among other additional factors behind the upsurge in interest, the recognition that the fatalistic attitude previously predominant concerning childhood cancer is no longer valid. Pack and Ariel also note this earlier misconception and cite a case in point with their 42 % five-year-cure rate in cases of sarcoma of the soft-somatic tissues of infants and children.

Whether, and where, a line should be drawn between the congenital cancer and that of early infancy is a thorny question. One would have a hard time equating the metabolic and environmental conditions of a fetus to those of an adult. An area in which there seems to be some strength to an argument for non-differentiation of congenital vs. postnatal is in the case of neuroblastomas or in that of Wilms' tumors in which merely a delay in manifestation seems to be acceptable.

Ewing's idea that the decline of the childhood types of tumors in the period 8 to 15 years of age suggests an exhaustion of the causative factors of infancy with overlap then with precocious forms of adult tumor, seems still to properly state the case.

Dargeon cites the rarity of fetal tumors in noting the occurrence of but two tumors, and these but choriangiomas, in a series of 54,429 deliveries. He also cites Potter's sole malignant tumor in a series of 60,000 deliveries.

This meristoma has no evident parallel in the literature. Pack and Ariel believe that "... many neoplasms catalogued as tumors of unknown histogenesis may be reported as fibrosarcomas in reports from other institutions." With this possibility in mind we can search further in the literature with the assumption that a tumor of similar nature may be in the literature as "sarcoma". Other possibilities for recording past tumors of similar nature may be embodied in Willis' proposal "... a tumor may be so lacking in differentation that even the epithelial nature (he was speaking here of thyroid) of its cells cannot be inferred from its structure or arrangement; the histologist alone can identify it then as 'a highly cellular anaplastic tumor of undetermined origin'."

With the two above possibilities in mind the following must be considered. Pack and Ariel point out the scarcity of sarcomas in the neck and numerous authors point out the preponderance of sarcomas over carcinomas in the child in opposition to the relationship in the adult. Mayo and Lee reported but one sarcoma in the neck in a series of 304 malignant neoplasms in which 103 were metastatic to the neck. Our tumor, again, was primary in the neck. Neel, who had hoped to throw some light on branchial cancer with his careful study of the pathological specimens from the 319 cases of branchial cysts and sinuses removed in the Mayo-Clinic, found none. The four cases of Carp and Stout have another histology (epitheliomas). Ladd and Gross in their

series of 82 cysts, fistulas, and cartilaginous cutaneous tabs believed to be of branchial origin, had no carcinomas.

Dargeon in his tabulation of the Memorial Center Series (the first Children's Tumor Registry, established in 1939) classified five tumors as "unclassified" out of 59 soft parts tumors in the total 233 juvenile head and neck tumors. Wells did list three of his cases of congenital tumor from the literature as "undetermined nature".

This use of "unclassified" and "undetermined nature" are so nebulous as to give no help in relating our tumor. Dargeon's five were not fetal tumors, but there again is the question of where one will draw the line.

In short, the tumor described, with its several facets—fetal malignant tumor, meristoma type, and branchial origin—seems to represent a unique case.

Summary

1. A congenital malignant tumor of branchial origin, with autopsy, is described.
2. The meristoma class of tumors is discussed.
3. Branchial origin of malignant tumors is discussed.
4. Malignant tumors of the fetus and of the very young are discussed.

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